

The difference between the prior art and the instant claims is "the substituent at the 4-position of the isoxazole" ( $R^2$  in the instant claims) as the Examiner pointed out.

Applicant discloses comparison data between a compound wherein  $R^2$  is hydrogen and a compound wherein  $R^1$  is alkyl (methyl) in Test Example 1 at page 264 to 265 of the specification. See Table 166. In Table 166, the compound wherein  $R^2$  is hydrogen is "Reference compound" and the compound wherein  $R^2$  is methyl is  $\beta$ -1-3. The structure of  $\beta$ -1-3 is disclosed in Table 79 at page 183 of the specification. The difference between the reference compound and  $\beta$ -1-3 is only  $R^2$ . Table 166 shows the EC50 values for PPAR $\delta$  activity of both compounds. The EC50 value of  $\beta$ -1-3, which is a value of 9.9, is low. On the other hand, the EC50 value of the reference compound, which is a value of 37, is much higher than that of  $\beta$ -1-3.

These results show that the PPAR $\delta$  activity of  $\beta$ -1-3 is much stronger than that of the reference compound. The inventors of this invention surprisingly found that, as to these species, compounds with the claimed substituents at the 4-position of the isoxazole are unexpectedly better as a medicine than compounds in which  $R^2$  is hydrogen. The reference does not disclose or suggest this discovery. Therefore Applicants submit that the species rejected by the Examiner in claims 1, 2, 4-10 and 26 is patentable and not obvious over the cited reference.

In view of the foregoing, it is believed that each ground of rejection set forth in the Official Action has been overcome, and that the application is now in condition for allowance. Accordingly, such allowance is solicited.

Respectfully submitted,

Yoshikazu FUKUI et al.

By: Warren M. Cheek  
Warren M. Cheek  
Registration No. 33,367  
Attorney for Applicants

WMC/dlk  
Washington, D.C. 20006-1021  
Telephone (202) 721-8200  
Facsimile (202) 721-8250  
May 22, 2008